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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/699,562 | 10/31/2003 | Tao Jiang | 02307E-161500US | 1597 |

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| EXAMINER | |
|---|---|
| JONES, DAMERON LEVEST | |
| **ART UNIT** | **PAPER NUMBER** |
| 1618 | |

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/699,562 | JIANG ET AL. | |
| | Examiner | Art Unit | |
| | D. L. Jones | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *9/13/06; 6/15/05; & 1/13/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *42 and 49-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41,43-48 and 54-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/12/05* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 1/13/05 wherein the specification was amended.

***Note***: Claims 1-56 are pending.

## RESPONSE TO APPLICANT'S ELECTION

2. The Examiner acknowledges Applicant's election of Group I (claims 1-41, 43-48, and 54-56 drawn to molecular products comprising A-X-B wherein SEQ ID No. 1, PLGLAG, is utilized) with traverse in the response filed 9/13/06. In addition, Applicant elected the species of SEQ ID No. 13. In summary, the traversal is on the grounds that restricting a single claim into more than one group is improper; searching the claims together would not present an undue burden on the Examiner, and the Examiner has not provided any reasoning to show why examining the claims would lead to a burdensome search of the art. Applicant's arguments are found non-persuasive for the reasons of record in the office action mailed 7/13/06 and those set forth below. First, the restriction requirement was made on the basis that the instant application contained various patentably distinct inventions. In addition, the restriction is deemed proper because each of the sequences disclosed in the instant invention is structurally different. According to MPEP 808.02 restriction is proper when there is a serious burden on the Examiner if restriction was not required. A serious burden exists in the instant application because searching different classes/subclasses is necessary depending on the number of amino acids present in the peptide. For example, the

instant invention read on tripeptides which classify in 530/331; peptides with 4-5 amino acids in the sequence classify in 530/330; peptides with 6-7 amino acids in the sequence classify in 530/329; peptides with 8-10 amino acids in the sequence classify in 530/328; peptides with 11-14 amino acids in the sequence classify in 530/327; peptides with 15-23 amino acids in the sequence classify in 530/326; peptides with a radiolabel classify in 424/1.69, etc. Therefore, the peptides are structurally different and require different search queries. Furthermore, review of Applicant's claim, for example, independent claim 1 indicates that 5-20 basic amino acids (i.e., His, Lys, Arg, and combinations thereof) may be present along with 2-20 acidic amino acids (i.e., Asp, Glu, Asn, Gln, and combinations thereof). In addition, the molecular product of claim 1 has 2-100 atoms that may link A to B. Also, according to MPEP 808.02, the Examiner does not have to show that Applicant's invention requires (a) a separate classification; (b) a separate status in the art; ***and*** (c) a different field of search. MPEP 808.02 specifically states that 'the Examiner must show by appropriate explanation ***one***' of (a), (b), or (c) above. Thus, the Examiner has fulfilled the requirement of showing why searching the full scope of the invention is a burden on the Examiner. Hence, the restriction requirement is deemed proper and is made FINAL.

***Note***: Initially, Applicant's elected species was searched. However, since no prior art was found which could be used to reject the elected species, the search was expanded over the full scope of Group I which is directed to molecular products comprising SEQ ID No. 1, PLGLAG. Applicant is respectfully requested to cancel all non-elected subject matter.

**WITHDRAWN CLAIMS**

3. Claims 42 and 49-53 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

**STATUTORY DOUBLE PATENTING REJECTION**

4. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5. Claim 11 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 21 of copending Application No. 11/133,804. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

6. Claim 11 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 21 of copending Application No. 11/437,095. This is a

provisional double patenting rejection since the conflicting claims have not in fact been patented.

**112 FIRST PARAGRAPH REJECTION (Prevention Claims)**

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-41, 43-48, and 54-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The instant invention is directed to peptide complexes and uses thereof that prevent cellular uptake. The peptide complexes may be used for various purposes including delivery of an imaging contrast agent or anti-proliferative agent as cargo to cancer cells (see Applicant's published application, US 2005/0107583, page 3, paragraph [0024]).

(2) State of the prior art

The state of the prior art for peptides useful for cancer therapy, for example, remains highly unpredictable. The various types of cancers cells have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol; thus, peptides that prevent cellular uptake of various components are not well known in the art. It is known (see Golub et al., Science, October 15, 1999, pp. 531-537) that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types in order to maximize efficacy and minimize toxicity. The classification of cancer has been based primarily on morphological appearance of the tumor and that of tumors with similar histopathological appearance may follow significantly different clinical courses and have different responses to therapy (see Golub et al., Science, October15, 1999, pp. 531-537). As a result, there is no absolute predictability of which tumors are treatable or that cellular uptake of a given component is preventable, even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the knowledge in the art would hinder one of ordinary skill in the art from accepting any therapeutic regimen as being acceptable for all tumor/cancer treatments.

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. There is no evidence of record which would enable the skilled artisan in the identification of the components which are prevented from cellular uptake within a subject who have the potential of becoming afflicted with the numerous diseases or disorders that are encompassed by the instant invention. The assumption that a peptide comprising a portion A that is about 2 to about 20 acidic amino acid linked by about 2 to about 100 atoms to a portion B that is about 5 to about 20 basic amino acid residues may be prevented from cellular uptake is an incredible finding for which Applicants have not provided supporting evidence. Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the complexes used in preventing cellular uptake as claimed.

(4) Level of predictability in the art

The art pertaining to the prevention of any condition (i.e., cellular uptake) is highly unpredictable. Determining the various types or classes of conditions/diseases involving cells wherein cellular uptake is prevented requires various experimental procedures and without guidance that is applicable to all cells and conditions/diseases, there would be little predictability in performing the claimed invention.

(5) Amount of direction and guidance provided by the inventor

There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the numerous diseases/conditions claimed herein wherein cellular uptake using the complexes of the instant invention are prevented. Applicant's limited guidance does not

enable the public to prepare such a numerous amount of complexes for preventing cellular uptake. There is no directional guidance for the types or classes of cells wherein the complexes of the instant invention result in the prevention of cellular uptake. The evidence of record does not provide as to exactly what cellular type of cellular uptake is prevented. Hence, there is no enablement for prevention of all possible cellular uptake using the complexes of the instant invention.

(6) Existence of working examples

The independent claims encompass a vast number of cell types. Applicant's limited working examples do not enable the public to prepare such a numerous amount complexes which prevent cellular uptake.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible cell types known to exist. For example, there are may types of cells such as acidophilic, acinar, adipose, alpha cell of pancreas, alveolar, amacrine, anaplastic, aneuploid, antigen sensitive, argentaffin, balloon, band, basal, basophil cell of anterior lobe of hypophysis, beta cell of anterior lobe of hypophysis, Betz, bipolar, blast, blood, bur, cartilage, stomach, parathyroid gland, chromaffin, chromophobe, columnar, cone, endothelial, epithelial, etc. that are known to exist.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the

specification fails to enable the skilled artisan to practice the invention without undue experimentation. Furthermore, based on the unpredictable nature of the invention, the state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

**112 SECOND PARAGRAPH REJECTIONS**

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-41, 43-48, and 54-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-41, 43-48, and 54-56: The claims as written are ambiguous because it is unclear what linkers have about 2 to about 100 atoms Applicant is referring to which can be cleaved under physiological conditions. In other words, it is unclear what particular linkers Applicant is referring to that are compatible with the instant invention such that the desired results are yielded.

Claims 1-41, 43-48, and 54-56: The claims as written are ambiguous because it is unclear what Xaa is in the sequences (SEQ ID No. 13). Applicant is respectfully requested to clarify what is meant by 'Xaa' and point to page and line number where support may be found for such terminology.

**COMMENTS/NOTES**

11. It should be noted that no prior art has been cited against the instant invention. However, Applicant MUST address and overcome the double patenting and 112 rejections above. In particular, the claims are distinguished over the prior art of record because the prior art neither anticipates nor renders obvious molecular products as set forth in independent claims 1, 11, and 46 comprising SEQ ID No. 1.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. L. Jones
Primary Examiner
Art Unit 1618

November 27, 2006